Solubility of Plant Constituents

- Content sourced from "Solubility_of_Constituents.pdf" by Lisa Ganora

Polarity of Solvent Solutions

- Water 80
- Ethanol 25
- Glycerol 46
- The overall polarity of a solvent mixture depends on the ratios of ethanol and water (and glycerin, if you are using it) in it. Adding glycerine (glycerol) could either raise the overall polarity of an ethanol/water solvent mixture, or could lower it, depending on this ratio. One way to measure the polarity of a compound is to give it a number called the 'dielectric constantl
- Websites with table of relative polarities, densities, etc. for organic solvents: http://www.iqo.csic.es/pagperso/afm/disolven.htm#TABLE%202 and http://www.speckanalytical.co.uk/products/Tips/bps.html.
  This page has a good not-too-technical explanation of how polarity works: http://palimpsest.stanford.edu/byauth/burke/solpar/solpar4.html It's from this paper on solvent theory: http://palimpsest.stanford.edu/byauth/burke/solpar/
- You can determine the polarity of a solvent mixture by multiplying the volume fraction of each solvent times its dielectric constant and summing. For example:
- If you are using 50% ethanol and 50% water, without any glycerol, your overall polarity would be 52.5: (.50)(25) + (.50)(80) = 52.5
- if you are using 50% ethanol, 45% water, and 5% glycerol, your overall polarity would be (.50)(25) = (.45)(80) = (.05)(46) = 12.5 + 36 + 2.3 = 50.8. So in this case replacing 5% of the *water* with glycerol would decrease the overall polarity of the mixture.
- What if you replaced 5% of the *ethanol* rather than 5% of the water with glycerol? The overall polarity would be 53.55. So in this case you have increased the polarity of the mixture (relative to just ethanol + water).

Relative polarity of the common solvents used in herbal extraction:

- Water 1.00
- Glycerol (glycerin) 0.812
- Ethanol (EtOH) 0.654
- Mixing water and ethanol together (hydroethanolic), in different proportions, determines the overall polarity of the solvent mixture. The higher the water percentage and the lower the ethanol, the higher the overall polarity (since water is more polar than ethanol). Conversely, the lower the water percentage and the higher the ethanol, the lower the overall polarity will be (since ethanol is less polar than water). So a 24 % EtOH tincture would have 76 % water and would be very polar, while a 95 % EtOH tincture would have only 5 % water and would be much less polar.
  For detailed solubility of individual, isolated molecules, consult the Merck Index (Merck & Co., Inc., Whitehouse Station, NJ).
  Solubility in a given solvent is influenced by the polarity of a molecule's skeleton and functional groups, the molecular size, temperature, the pH of the solution, and other factors. The solubility of an isolated compound is easy to determine, but this may change in the complex matrix of a medicinal plant extract. The general principle: like dissolves like. A high-polarity solvent will pull high-polarity molecules out of the herbal material; a low-polarity solvent will select for low-polarity molecules.

Terpenoids (terpene compounds)

- *As a general rule, terpenoids tend to be oil and high-percentage ethanol soluble. Triterpene and steroidal saponins are water soluble because of their sugar groups. The smaller terpenoids (in essential oils) have very limited solubility in water, and are soluble in fixed oils and ethanol. Small terpenes include*
- **Hemiterpenes**
- **Monoterpenes**
- **Sesquiterpenes**
- *The larger terpenes are not volatile and tend to be oily or resinous substances. In general, they are soluble in fixed oils or high percentage ethanol. Many resinous materials are composed of larger terpenes (and/or polyphenolic aglycones)*
- **Diterpenes**
- **Triterpenes**
- **Tetraterpenes** (carotenoids)
- *The aglycones of triterpenoid saponins (sapogenins) are practically insoluble in water or ethanol, while their glycosidic forms are highly water soluble and amphiphilic (soapy/foamy).*

Lipids/Oil Soluble

- *Lipids are generally soluble in other lipids*
- *Essential oils are not lipids, but rather are composed mainly of small terpene compounds; soluble in mid- to high-percentage ethanol, fixed oils, slightly soluble in water*
- **Fatty acids** (e.g. Omega 3s, EFAs, PUFAs, DHA, EPA): mostly oil soluble, slightly soluble in ethanol
- **Triglycerides** (triacylglycerols; fixed oils such as Olive or Almond are mostly composed of triglycerides): very slightly soluble in ethanol, not in water, and will dissolve many oil soluble compounds
- **Phospholipids** (e.g. lecithin, phosphatidyl choline, PS): are emulsifiers
- **Waxes** (e.g. beeswax): soluble in warm oils but not in cold
- **Alkamides** (e.g. the tingly isobutylamides in *Echinacea spp.* & *Acmella oleracea*): soluble in 40–60% ethanol
- **Polyacetylenes** (e.g. arctinal from *Arctium lappa*; PHT from Bidens): similar to alkamides
- **Unsaponifiable matter** (anything dissolved in an oil, such as olive, which is not a fatty acid or triglyceride; includes oil-soluble vitamins, phytosterols, carotenoids, etc.)

Steroids

- *Plant steroids are oil-soluble, with the exception of glycosidic forms (e.g. steroidal saponins and cardiac glycosides); the latter are slightly water soluble*
- **Phytosterols**: soluble in fixed oils and high percentage ethanol
- **Steroidal saponins**: aglycones are not water soluble; glycosidic forms are
- **Cardiac glycosides**: slightly water soluble; more so in dilute alcohol; aglycones are oil soluble

Amino Acids & derivatives

- *Proteins and enzymes denature in ethanol*
- *Tannins can bind and precipitate proteins*
- **Free amino acids** at pH 7 are zwitterions very water soluble, generally soluble in low percentage ethanol
- **Some sulfur-containing amino acid derivatives** (e.g. ajoene and sulfides from *Allium sativum*): oil soluble, some sulfides have limited water solubility
- **Cyanogenic glycosides** (e.g. amygdalin, prunasin): soluble in water, more so in hot water, somewhat soluble in cold ethanol, more so in hot ethanol
- **Amines** like alkaloids: generally more soluble in acidic media; **amine salts** : water soluble (ionic)
- **Methylxanthines** (e.g. caffeine): hot water soluble, less so in cold water
- **Peptides** (e.g. glutathione): generally water soluble, depends on pH (lose solubility at isoelectric point)
- **Proteins**: generally water soluble, depends on pH (lose solubility at isoelectric point)
- **Enzymes**: generally water soluble, depends on pH (lose solubility at isoelectric point)

Carbohydrates/ Water Soluble

- *Carbohydrates generally stay dissolved in low-ethanol (20–30%) preparations and in glycerites*
- *Carbohydrates generally will precipitate out at higher ethanol ratios*
- *Tannins can bind to and precipitate complex carbohydrates*
- **Monosaccharides** (e.g. glucose, fructose): highly water soluble
- **Organic acids** (e.g. citric acid, formic acid): generally water soluble varies with pH
- **Disaccharides** (e.g. sucrose, maltose): highly water soluble
- **Oligosaccharides** (e.g. inulin, FOS): water soluble especially in hot water
- **Heteropolysaccharides** (e.g mucilages, gums): highly water soluble
- **Homopolysaccharides**
  - starch: hot water soluble
  - cellulose: insoluble
- **Dietary Fiber**
  - Soluble
    - includes heteropolysaccharides such as mucilages, gums, and pectins
  - Insoluble (e.g. cellulose, lignin)

Alkaloids

- The pH of the solution influences the solubility of alkaloids. In general, alkaloids are more oil soluble in high pH (alkaline) solutions. Conversely, they are more water soluble in acidic solutions. Most alkaloids are soluble in mid- to high-percentage ethanol/water solutions.
- **Capsaicinoids** (pseudo-alkaloids): oil soluble
- The purple and yellow betalain alkaloids (found in beets, pokeberries, prickly pear cactus, amaranth, etc.) are very soluble in water and will remain dissolved in low- to mid-percentage ethanol solutions.
- The isoquinoline alkaloids are soluble in moderate- to high-ethanol solutions with the exception of berberine, which is far more water soluble than the others.
- The N-oxide forms of pyrrolizidine alkaloids (PAs) are very water soluble. PAs are soluble in low-pH solutions, but insoluble in high-pH solutions. They are also soluble in ethanol and in organic solvents such as acetone. They are nearly insoluble in fixed oils.

Phenolic Compounds

- *Structures of phenolic compounds (polyphenols) vary widely, and many can occur as either glycosides or aglycones. Glycosides are generally more water soluble than the aglycones. Depending on pH, the hydroxyl groups may be ionized; this enhances water solubility.*
- **Phenolic acids**: solubility varies with structure and pH
- **Phenylpropanoids**: solubility varies with structure and pH
- **Coumarins**: glycosidea generally water and ethanol soluble; aglycones less so
- **Lignans**: generally soluble in acetone/water (Flaxseed lignans are not oil soluble)
- **Phenylpropanoid derivatives** (e.g. capsaicin, curcumin, gingerol): soluble in high percentage ethanol and fixed oils
- **Stilbenoids** (e.g. resveratrol): soluble in ethanol
- **Xanthones**: generally soluble in ethanol and fixed oils
- **Styrylpyrones** (e.g. kavalactones): soluble in high percentage ethanol and acetone)
- **Isoflavonoids**: soluble in ethanol; low water solubility; however, glycosidic forms are more water soluble
- **Benzofurans** (e.g. usnic acid): soluble in hot ethanol; solubility in water and ethanol is very low
- **Chromones** (e.g. khellin): soluble in hot water and hot ethanol
- **Quinones** (e.g. anthraquinones): solubility varies; most soluble in water and ethanol; bianthraquinones in *Hypericum perforatum* are oil soluble.
- **Phloroglucinol derivatives** (e.g. hyperforin, cannabinoids): soluble in oil and high percentage ethanol
- **Flavonoids**: solubility varies, but many are water and ethanol soluble
  - **Anthocyanins**: water and ethanol soluble
  - **OPCs**: water and ethanol soluble
  - **Tannins**: smaller tannis soluble in hot water and ethanol; larger tannins relatively insoluble

Quick Reference

- adapted from *The Modern Herbal Dispensatory* by Thomas Easley and Steven Horne and *The Herbal Medicine-Maker's Handbook* by James Green
- Water
  - Aromatic Bitters (sesqueterpene lactones and triterpenes) GOOD
  - Simple (nonalkaloidal) Bitters (diterpenes, glycosides) GOOD
  - Alkaloidal Bitters (alkaloids) GOOD
  - Acrid Herbs (resins, alkaloids) GOOD
  - Astringent Herbs (tannins) GOOD
  - Salty Herbs (minerals) EXCELLENT
  - Sweet or Tonic Herbs (polysaccharides, saponins, glycosides) EXCELLENT
  - Demulcent Herbs (mucilage and gums) GOOD
  - Sour Herbs (organic acids) GOOD
- Ethanol
  - Aromatic Herbs (essential oils) GOOD
  - Pungent Herbs (alkamindes) EXCELLENT
  - Pungent or Resinous Herbs (resins) EXCELLENT
  - Aromatic Bitters (sesquiterpene lactones and triterpenes EXCELLENT
  - Simple (nonalkaloidal) Bitters (diterpenes, glycosides) EXCELLENT
  - Alkaloidal Bitters (alkaloids) GOOD
  - Acrid Herbs (resins, alkaloids) EXCELLENT
  - Sweet or Tonic Herbs (polysaccharides, saponins, glycosides) GOOD
  - Sour Herbs (organic acids) GOOD
- Glycerin
  - Aromatic Herbs (essential oils) EXCELLENT
  - Pungent Herbs (alkamindes) EXCELLENT
  - Acrid Herbs (resins, alkaloids) GOOD
  - Astringent Herbs (tannins) EXCELLENT
  - Sweet or Tonic Herbs (polysaccharides, saponins, glycosides) GOOD
  - Sour Herbs (organic acids) EXCELLENT
- Vinegar
  - Aromatic Herbs (essential oils) GOOD
  - Pungent Herbs (alkamindes) GOOD
  - Alkaloidal Bitters (alkaloids) GOOD
- Oil
  - Aromatic Herbs (essential oils) EXCELLENT
  - Pungent Herbs (alkamindes) EXCELLENT
  - Pungent or Resinous Herbs (resins) EXCELLENT
  - Oily Herbs (oils) EXCELLENT